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CDC HEALTH UPDATE

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Response to Questions Raised by State Health Officers

To State Health Officers, State Epidemiologists and State Laboratory Directors

- **I. Status of the Investigation**

Since October 3, 2001 CDC has been investigating two human cases of anthrax or *B. anthracis* infections. The first case involved inhalational anthrax in a 63-year-old male in Florida, and the second was a case of cutaneous anthrax in a 35-year-old female in New York City. Specimens from these patients were confirmed at CDC as positive for *B. anthracis*. Teams of CDC investigators were sent to both locations to assist state and local authorities in an epidemiologic assessment of exposures and environmental contamination.

This report covers the following topics that pertain to public health investigations where *B. anthracis* is suspected to have been employed as a bioterrorist threat: law enforcement and public health approaches to the investigation of suspicious letters and/or packages and/or the environment, laboratory analysis of human and environmental specimens obtained, and prophylactic use of antibiotics. Updates on the status of the current investigation can be obtained through CDC's Bioterrorism website (internet address: www.bt.cdc.gov).

II. Laboratory and Other Resources

Each State should review its State bioterrorism preparedness plans and its access to the Laboratory Response Network for Bioterrorism (LRN). LRN is a collaborative partnership and multilevel system designed to link state and local public health laboratories with advanced capacity laboratories - including clinical, military, veterinary, agricultural, water and food-testing laboratories - for rapid identification of threat agents including *B. anthracis*.

CDC's BT public website: emergency.cdc.gov provides access to CDC's Centers for Public Health Preparedness, a national network of academic institutions and local health departments whose goal is to ensure that local public health workers are fully prepared to respond to current and emerging health threats, including bioterrorism.

III. Responding to Suspicious Letters and Packages

Guidance for responding to suspicious letters and packages has been detailed in the official CDC Health Advisory, "How to Handle Anthrax and Other Biological Agent Threats" (see resource web site below). Readers are referred to this Advisory for details, although some key points are summarized below.

Characteristics of suspicious letters or packages include:

- Excessive postage
- Handwritten or poorly typed addresses

- Incorrect titles
- Title, but no name
- Misspellings of common words
- Oily stains, discolorations, or odor
- No return address
- Excessive weight
- Lopsided or uneven envelope
- Protruding wires or aluminum foil
- Excessive security material (e.g., masking tape, string)
- Visual distractions
- Ticking sound
- Marked with restrictive endorsements (e.g., ∟Personal∟ or ∟Confidential∟)
- Postmark with city / state not matching return address

CDC has recommended that for suspicious unopened letters or packages:

- Do not shake or empty the contents.
- Place the envelope or container in a plastic bag or some other container.
- If a container is not available, then cover the letter or package.
- Leave the room and close the door.
- Wash hands with soap and water.
- If at home, report the incident to local police. If at work, report the incident to local police and notify building security or an area supervisor.
- List all people present in the room or area when the letter or package was recognized.

For all settings, law enforcement authorities determine the credibility of suspicious letters, packages, and other potential threats.

- A law enforcement official or public safety responder arrives at the scene.

- The responder may then contact the FBI, which evaluates the information and makes a determination regarding the credibility of the threat.

If law enforcement determines that the threat is credible:

- Any suspected isolate of *B. anthracis* must be reported to the State Public Health Laboratory IMMEDIATELY.
- If analysis of the specimen yields a positive culture for *B. anthracis*, then antibiotic prophylaxis may be indicated for those persons exposed to letter or package, and possibly other persons in immediate area
- If the threat is determined not to be credible, then law enforcement assessment continues, but no prophylaxis administered.
- Resource: http://www.bt.cdc.gov/DocumentsApp/Anthrax/OfficialCDCHealthAdvisoryOct122001

IV. Evaluating and Managing An Exposed Environment

The response to evaluating and managing an exposed environment is highly contingent upon the specific situation

- First, determine the nature of the threat. If a package is received intact and law enforcement considers it to be a creditable threat, then law enforcement will determine which portions of the building should be secured and how long access will be restricted.
- Law enforcement will make this determination since the area is considered a crime scene. Advice from public health officials may be sought in the decision process.
- For intact letters and packages, the restricted area is likely to be limited and the duration of the restriction may be commensurately limited.
- For letters and packages not intact, the restricted areas may be expanded to include those areas where the contents may have discharged into the environment.
- Other factors to be considered in determining the boundaries of the restricted area include air handling systems, tracking of the contaminant by people moving through the area, and other transport means.
- The areas are restricted generally until laboratory analysis can be completed.
- If environmental sampling results reveal that the presence of *B. anthracis* poses an ongoing threat, federal response plans may be activated to address the issue of cleanup of the contaminant.
- The Environmental Protection Agency has lead responsibility for environmental issues with the assistance of 16 federal agencies and departments, including CDC.
- Federal agencies, in conjunction with State and local agencies, will determine the most efficient approach to the cleanup based upon factors including sampling results, review of cleanup options, and the environmental situation.

- Qualitative identification of *B anthracis* from environmental specimens may include:
- Analysis for spores using wet mount and malachite green staining.
- Isolation of the organism on sheep blood agar (DFA testing, colony morphology, gram stain, hemolysis, and motility, Gamma phage).

V. Nasal Swabs and Screening for Exposure to *Bacillus anthracis*

- Nasal swab screening may assist in epidemiologic investigations, but not should not be relied upon as a guide for prophylaxis or treatment.
- At present, CDC does not recommend the use of nasal swab testing on a routine basis to determine whether a person has been exposed to *B. anthracis* or as a diagnostic tool.
- Epidemiologic investigations in response to threats of exposure to *B. anthracis* may employ nasal swabs of potentially exposed persons as an adjunct to environmental sampling to determine the extent of exposure.
- A collection swab is used to sample the anterior nasal passage; following inoculation into a culture medium and incubated overnight, preliminary results may be available in a minimum of 12 hours.
- A study of persons with occupational exposure to *B. anthracis* reported in 1957 indicated that nasal or pharyngeal carriage was confirmed among 14 (14%) of such workers (ref: Carr and Rew). Although a few of the workers were reported to have mild coryza, correlations of carriage with such symptoms were not given. None of the workers were reported to have manifestations of advanced infection.
- Timed recovery of *B. anthracis* spores from eight previously vaccinated or immune macaques was studied under controlled, experimental conditions (ref: Hail et al.). Spores were recovered from nares samples at 0-, 1-, and 4-hour time points. At 24 hours, spores were detectable in small quantities, and at one week, spores were detected in only one of the 8 macaques. However, because this study was conducted under tightly controlled conditions and using macaques, the results should not be directly extrapolated to humans.
- Nasal swabs may be useful as a tool for epidemiologic investigations and the results of such testing is subject to substantial limitations.
- Testing parameters (e.g., sensitivity, specificity) have not been defined.
- Results of this method are not a predictor for disease: correlations with infectivity, serologic (immune) status, and likelihood of disease occurrence are unknown.
- In particular, the sensitivity of this method for detecting exposure to *B. anthracis* spores is unknown - i.e., the ability of this method to correctly identify those who have been exposed has not been quantified.
- At best, a positive result may be interpreted only to indicate exposure.
- At worst, a negative result is not useful in any way.

- Nasal swabs have been used for epidemiologic assessment in the ongoing investigations.
- In the Florida investigation, this method was used as a screening tool because, following the initial recognition of the case of confirmed inhalational anthrax, there were no suspected or known sources of exposure and it was important to begin attempts to determine whether anyone else associated with the case-patient might have been exposed. In this setting, the nasal swab method was used for a rapid assessment of exposure among persons and as a tool for rapid environmental assessment.

References:

- Carr EA and Rew RR. Recovery of *Bacillus anthracis* from the nose and throat of apparently health workers. J Inf Dis 1957; 100: 169-71.
- Hail AS, Rossi CA, Ludwig GV, et al. Comparison of noninvasive sampling sites for early detection of *B. anthracis* spores from rhesus monkeys after aerosol exposure. Military Med 1999; 164:833-37.

VI. Laboratory Analysis of Patients' Clinical Specimens

- In persons who are clinically ill, preferred sites for collection of clinical specimens are: vesicular fluid from a skin lesion, blood, cerebrospinal fluid, sputum, and stool.
- Isolation of *B. anthracis* from clinical specimens processed through LRN laboratories:
- The likelihood of isolating an organism is optimal if the patient has not yet been treated with antibiotics.
- Presumptive identification to identify to Genus level (*Bacillus* family of organisms) requires Gram stain and colony identification.
- Presumptive identification to identify to species level (*B. anthracis*) requires tests for motility, lysis by gamma phage, capsule production and visualization, hemolysis, wet mount and malachite green staining for spores.
- Confirmatory identification of *B. anthracis* carried out by CDC may include phage lysis, capsular staining, and direct fluorescent antibody (DFA) testing on capsule antigen and cell wall polysaccharide.
- Other diagnostic tests under development include
- Polymerase chain reaction (PCR) may have utility for rapid detection and diagnosis.
- Serologic assays (see below).
- Serologic testing is in development currently at CDC.
- Serologic tests for anthrax may be capable of determining the existence and functional ability of anthrax antibodies in persons vaccinated with anthrax vaccine.
- Enzyme Linked Immunoabsorbent Assay is the quantitative assay for antibody.

- Toxin Neutralization Assay determines the ability of anthrax antibodies to neutralize lethal toxin, one of the toxins of *B. anthracis* (functional assay).
- Potential uses of serologic testing may include assessment of protection conferred by the currently licensed anthrax vaccine.
- The ability of these tests to detect anthrax antibodies in patients clinically ill with anthrax or those exposed to *B. anthracis* spores is currently being assessed.

VII. Prophylactic Use of Antibiotics

- Antibiotic prophylaxis should be initiated following confirmed or suspected exposure to *B. anthracis.*
- Three antibiotic agents are approved by the FDA for treatment: penicillin, doxycycline, and ciprofloxacin.
- Currently, ciprofloxacin is the only antibiotic approved by the FDA for use in reducing the incidence or progression of disease after exposure to aerosolized *B. anthracis* (i.e., inhalational anthrax).
- Facts about ciprofloxacin (cipro):
- A broad-spectrum, synthetic antimicrobial agent active against several microorganisms.
- Prevents the development or progression of inhalational anthrax.
- Adverse health effects include: vomiting, diarrhea, headaches, dizziness and rashes.
- Hypertension, blurred vision and other central nervous system effects occur in less than 1% of patients.
- The use of ciprofloxacin is warranted only under the strict supervision of a physician.
- Indiscriminate use of ciprofloxacin and other antibiotics can contribute to antimicrobial resistance and lessen the effects of these agents against many infections.
- Inappropriate accumulation of stocks of CIPROFLOXACIN may threaten the supply of this antibiotic in imminent circumstances.
- Recommendations for use of ciprofloxacin and doxycycline for post-exposure prophylaxis following exposure to *B. anthracis*:

	Initial therapy	**Duration**
Adults (including pregnant woman [1,2] and immuno-compromised)	Ciprofloxacin 500 mg po BID **Or** Doxycycline 100 mg po BID	60 days

Children [1,3]	Ciprofloxacin 15-20 mg/kg po Q12 hrs [4] **Or** Doxycycline [5]: >8 yrs and >45 kg: 100 mg po BID >8 yrs and # 45 kg: 2.2 mg/kg po BID # 8 yrs: same as >8 yrs and # 45 kg	60 days

If susceptibility testing allows, therapy should be changed to oral amoxicillin for post-exposure prophylaxis to continue therapy out to 60 days.

Although tetracyclines are not recommended during pregnancy, their use may be indicated for life-threatening illness. Adverse affects on developing teeth and bones are dose related, therefore, doxycycline might be used for a short course of therapy (7-14 days) prior to the 6th month of gestation. Please consult physician after the 6th month of gestation for recommendations.

Use of tetracyclines and fluoroquinolones in children has adverse effects. These risks must be weighed carefully against the risk for developing life-threatening disease. If a release of *B. anthracis* is confirmed, children should be treated initially with ciprofloxacin or doxycycline as prophylaxis but therapy should be changed to oral amoxicillin 40 mg/kg of body mass per day divided every 8 hours (not to exceed 500 mg three times daily) as soon as penicillin susceptibility of the organism has been confirmed.

Ciprofloxacin dose should not exceed 1 gram/day in children.

In 1991, the American Academy of Pediatrics amended their recommendation to allow treatment of young children with tetracyclines for serious infections, such as, Rocky Mountain Spotted Fever, for which doxycycline may be indicated. Doxycycline is preferred for its twice-a-day dosing and low incidence of gastrointestinal side effects.